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13. ABSTRACT (Maximum 200 Words)

The **purpose** is to evaluate perioperative training for lymphedema protection. The **hypothesis** is that structured perioperative training in lymphedema protection will decrease lymphedema, and improve the QOL in patients undergoing axillary dissection and/or radiation therapy for breast cancer as compared to a control group. The **specific questions** are 1) what is the incidence of lymphedema and infection during the first three years after surgery among breast cancer patients who received perioperative training in lymphedema protection as compared to a control group? 2) What are the differences in the measured QOL among these breast cancer survivors? 3) What are the retention of information on lymphedema protection, and the compliance with arm precautions among these breast cancer survivors? **Major Findings:** In this interim report, the LE rate is 55%. Our rate for acute LE is 46.2%. Presentation of LE after the first year after surgery occurred in 8.9% of the study patients. There were 38.6% acute LE cases persisting to become chronic for a total chronic rate of 47.5%. **Significance:** LE is a significant problem. The identification of newer treatment plans and modalities that may obviate the need for injury to the lymphatics would help reduce the incidence of LE.

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INTRODUCTION

Narrative:

Subject: Increasing numbers of breast cancer survivors are at risk for long-term sequelae from treatment. Axillary surgery or radiation therapy to the breast may alter lymph channels, leaving the survivor with a lifetime risk for developing lymphedema. Lymphedema is a swelling of the upper extremity, which causes pain, debility, and reduced quality of life (QOL) that impacts choices about work, social and sexual interactions and self-esteem. Protective measures to reduce the risk of lymphedema become important life-long skills. However, there is inconsistent teaching of protective measures, and inattention to lymphedema detection in clinical practice. **Purpose:** The purpose of this study is to test that structured perioperative training in lymphedema protection will decrease lymphedema, the episodes of infection, the time to detection of lymphedema and improve the QOL in patients undergoing axillary dissection and/or radiation therapy for breast cancer as compared to a control group. **Scope:** The specific aims are 1) what is the incidence of lymphedema and infection during the first three years after surgery among breast cancer patients who received perioperative training in lymphedema protection as compared to a control group? 2) What are the differences in the measured QOL among breast cancer patients during the first three years after surgery that received perioperative education in lymphedema protection as compared to a control group? 3) What are the retention of information on lymphedema protection, and the compliance with arm precautions among breast cancer patients who received perioperative lymphedema training as compared to a control group? **Methods:** Patients with resectable breast cancer also undergoing axillary lymph node surgery and/or radiation therapy to the breast will be prospectively randomized to two groups. In addition to receiving standard care (i.e., written breast rehabilitation materials and preoperative counseling by the breast surgeon), patients in Group 1, will receive structured education in Breast Surgery Rehabilitation including range of motion exercises, lymphedema arm precautions, and management of complications. Patients in Group 2 will receive standard care (written material and preoperative counseling by the surgeon). For both groups, preoperative and then quarterly volume measurements and exams of the upper extremities will be done for three years after surgery in order to determine lymphedema and infection incidence. The QOL will be measured longitudinally by the Functional Assessment of Cancer Therapy-Breast (FACT-B) and the Medical Outcome Study Short Form Health Survey (MOS SF-36) and sexuality subscales of Cancer Rehabilitation Evaluation System (CARES). The knowledge of and practice of lymphedema protective skills will be measured by periodic testing longitudinally as well.

BODY

Part 1: Response to Reviewer's comments from Year III report:

Format/Editorial Issues

1. *"The Principal Investigator (PI) has commendably addressed each subtask in the approved Statement of Work (SOW), but has provided very little data to document progress or "complete accomplishment" of many subtasks."*

Response: In this report, data corresponding to specific subtasks are provided throughout to document the progress of accomplishment of the subtasks.

Subtask data is also presented as related to each of the Specific Aims of the study.

BODY (continued)

2. *"The PI states on page 13 that the lymphedema rate found among totally evaluable subjects (49.6%) is higher than that "predicted in the literature" (more properly, "expected on the basis of rates reported in the literature"), but fails to identify what rates (or range of rates) have been reported. This should not have been difficult, as the draft article (Bland, Perczyk et al.) included as supporting data provides both a reported range (6%-30%) and a source (Petrek JA and MC Heelan, Incidence of breast carcinoma-related lymphedema, Cancer 83:2776-2781 [1998]) that could easily have been included as a reference in the report."*

Response: In this report, if there are any references to the literature, specific data from the literature will be included for the convenience of the reviewers.

Technical Issues

1. "Interim data and statistical analysis of such data were missing in the report."

Response: In this report, interim data and statistical analysis of the data are included. We did not suffer a regional power outage as occurred last year.

Part 2: Research accomplishments associated with each task outlined in the approved Statement of Work. Therefore, the Year IV report is cumulative through 7/31/04

(Some figures and tables will be embedded in the text, others in the appendix.)

Task 1. **Start-up, Months 1-2.**
This was completely accomplished in 2000.

Task 2. **Introduce study to physicians, nurses and clerks in clinics, Months 1-2.**
This was completely accomplished in 2000.

Task 3. **Subject recruitment and data collection, Months 3-60.**

This is ongoing.
For Specific Aim 1, there are 158 evaluable patients which was the goal. This permits determination of interim LE and infection rates as the years of followup continue.
For Specific Aim 2, there are 153 evaluable patients since 5 did not complete the QOL questionnaires preoperatively, and will not be part of Spec. Aim 2 analysis. Interim determination of changes in QOL can be determined with this number while the followup continues.
For Specific Aim 3, there are 158 evaluable patients which permits determination of interim knowledge and compliance with LE protection measures while followup continues.

The data tables listed under ***Task 11*** show population and clinical characteristics of the study patients for the intervention and control groups for Specific Aims 1 and 3 (Tables 1 and 2)

ODY (continued)

Task 4. **Perioperative teaching sessions, Months 3-27.**

All patients randomized to the intervention group (n=71) underwent perioperative teaching by the LE study nurse, and underwent knowledge testing at the same time. See Appendix Item #1.

Task 5. **Quarterly measurements of subjects, Months 6-60.**

This is ongoing. Appendix Item #2 shows the measurement data of subjects in centimeters at multiple standardized sites along both upper extremities. If a patient is unable to complete a quarterly measurement, we see them at the next quarterly interval. See Appendix Item #2.

Task 6. **QOL questionnaires at 6 months, 1-, 2-, and 3-years postop, Months 9-60.**

This is ongoing. Tables 9 and 10 under ***Task 11*** show the population and clinical characteristics for the subjects for this group of data pertinent to Specific Aim 2. Interim analysis of the QOL data are shown under ***Task 11***.

Task 7. **Booster training session for Group 1 subjects, Months 9-33.**

Appendix #3 lists the booster sessions attended by the intervention group. Of the intervention group, 15 did not attend the booster session. Of these 6 are still within the timeframe to receive the booster session now. This leaves 9 (12.7%) without the booster session. The impact of the booster sessions is tested yearly by knowledge and compliance questionnaires as part of Specific Aim 3. From the original grant application:
"**Sample Size Calculation.** A total of 158 evaluable patients (79 in each arm) will be studied. This sample size will allow detection of a reduction in the acute lymphedema incidence rate from 25% to 10% with 80% power, 5% overall type I error, and a one-sided hypothesis test. It will also detect changes in the QOL measures using a 2-sided α at 0.05 and power at 0.8 for changes with $3/4^{th}$s of a standard deviation (43). Assuming an attrition rate of 10% due to dropouts, 176 patients will be needed to complete the accrual goal of 158 evaluable patients."

Therefore, we are continuing to evaluate eligible subjects so that 158 evaluable patients will have both the perioperative teaching (Task 4) and booster training (Task 7) completed.

Task 8. **Knowledge and compliance questionnaires, Months 9-60.**

This is ongoing. Interim data analysis is under ***Task 11*** for this item which tests Specific Aim 3.

Task 9. **Calculations of limb volumes and comparison of differences, Months 3-60.**

This is ongoing.
Weekly report sheets are created and reviewed which show cumulative data:

a) volume changes
b) >1cm measurement changes
c) Symptoms

Task 9 **(continued)**
All subjects with >10% volume change, >1cm measurement change and/or persistent symptoms are evaluated by the LE study nurse. Appendix # 4 shows a weekly volume report.

Task 10. **Quarterly data entry and print out by the Psychosocial and Behavioral Core, Months 3-60.**

This is ongoing. From the previous annual reports, the Psychosocial and Behavioral Core was dissolved by the reorganization at the Karmanos Cancer Institute. Data entry is now at least weekly by a data manager.

Task 11. **Interim analysis of data after 1 year, 3 years, Months 14-16, 38-40.**

The interim analysis of data is being reported in this Year IV report due to the power outage last August (2003) in our section of the US. We were excused for the Year III report.
The study statistician performed the interim analyses which are summarized in the following tables and figure. The comparisons of various patient characteristics between the control and intervention arm or between patients with and without lymphedema were performed using 2-sample t-tests and chi-square tests. A multivariable logistic regression with a backward variable selection procedure was also utilized to determine the relationship between lymphedema and various risk factors.

The interim data are reported according to the Specific Aims. Discussion about the data appears in between the data tables and figures.

Specific Aim 1) What is the incidence of lymphedema and infection during the first three years after surgery among breast cancer patients who received perioperative training in lymphedema protection as compared to a control group?

Table 1 Population Characteristics of Study Participants in the Intervention and Control Groups for LE Protection teaching (Specific Aim 1 and 3)

	Intervention Group	Control Group	Univariate
N	71	87	
Mean age, yrs ± S.D.	53.6 ± 11.8	52.8 ± 11.6	P=0.6671
Gender (F, M)	70, 1	86, 1	
Race			
African American	31	37	P=0.8862
Caucasian	33	38	
Hispanic	1	2	
Arab/Chaldean	1	2	
Asian	0	4	
Native American	3	1	
Other	2	3	
Highest education level			P=0.6838 For college vs no college
Less than high school	9	8	
High school/GED	36	43	
Associate degree	0	0	
Bachelor degree	13	16	
Masters degree	3	8	
Doctorate/professional school	3	1	
Not answered	7	11	
Annual income			P=0.4864 For < $50,000 vs ≥ $50,001
< $5,000	5	9	
$5,000-$15,000	9	12	
$15,001-$30,000	8	10	
$30,001-$50,000	8	8	
$50,001-$75,000	8	9	
> $75,001	16	15	
Not answered	17	24	
Marital Status			P=0.3438 For married/ cohabitating vs all others
Divorced/separated	17	17	
Married/Cohabitating	34	33	
Never married	8	11	
Widowed	8	16	
Not answered	4	10	
Religious Preference			P=0.1818 For Christian vs Non-Christian
Catholic	18	17	
Hindu	0	1	
Jewish	2	0	
Muslim	1	1	
Protestant	19	19	
Other	21	34	
None	2	4	
Not answered	8	11	
Transportation			P=0.5587 For drive myself vs all others
Usually drive myself	45	59	
Usually public transportation	8	1	
Usually driven	13	14	
Other	0	2	
Not answered	5	10	

Table 2 **Clinical Characteristics of Study Participants in the Intervention and Control Groups for LE Protection teaching (Specific Aim 1).**

	Intervention Group	Control Group	Univariate
N	71	87	
Breast Cancer Stage			P=0.9984
0	10	9	
I	21	29	Stage 0,I Vs Stage IIA, IIB, IIIA, IIIB, IV
IIA	17	19	
IIB	13	16	
IIIA	6	9	
IIIB	4	5	
IV	0	0	
Type of breast surgery)			P=0.8095
Mastectomy with axillary surgery	38	50	
Lumpectomy with axillary surgery	28	30	
Lumpectomy	5	7	
Radiation therapy			P=0.9984
Yes	40	49	
No	31	38	
Number of LNs resected (mean ± SD)	8.5 ± 5.8	9.9 ± 6.5	P=0.1786
≤ 8 LNs submitted	37	40	P=0.4428
> 8 LNs submitted	34	47	
Number of LNs positive for ca	1.1 ± 2.4	1.6 ± 3.0	P=0.2795
0	45	52	P=0.6332
1-3	19	22	
>4	7	13	
Body Mass Index (BMI) (mean ± SD)	29.3 ± 7.3	29.2 ± 7.6	P=0.9165
BMI >25	52	61	P=0.6651
BMI >30	27	35	P=0.7780

Discussion: From Tables 1 and 2, it can be concluded that the intervention and control groups of subjects are similar by univariate analysis. This is expected in a prospective randomized study. Therefore any differences in LE rate, infection, time to LE will be due to other reasons.

Table 3 **Incidence of LE in the intervention and control groups (interim data) (Specific Aim 1)**

	Secondary LE (n=87)	Without LE (n=71)	
Intervention (n=71)	42	29	P=0.3503
Control group (n=87)	45	42	

Table 4 **Infection rate in the intervention and control groups, and in those with LE and without LE (interim data) (Specific Aim 1)**

	Infection	No infection	
Intervention (n=71)	5	66	P=1
Control group (n=87)	3	84	
LE (n=87)	7	80	P=0.1
No LE (n=71)	1	70	

Discussion: From Table 3, the interim incidence of LE in the intervention group is not significantly different from the control group. From Table 4, the interim infection rate is similar in the intervention and the control group. However, there are more subjects with infection in the LE group than in the group without LE. The cases of infection may confound the effect of teaching and may need to be separated during the final analysis. Infection was predicted to increase the risk of LE[1].

To investigate whether there are any variables more strongly associated with LE, multivariate analysis was performed with this interim data. For multivariate analysis, stepwise logistic regression using the backward selection method was performed to determine association with LE by variables in the clinical or population characteristics. LE (yes/no) was dependent, and the other variables were explanatory variables. From Table 5, the highest correlation with developing LE was with any lymph nodes positive or the number of lymph nodes removed at surgery. Being Christian had a protective effect (odds ratio <1). Being in the control arm did not correlate with higher LE (or being in the intervention arm did not correlate with lower risk for LE). In Table 6 and Table 7, the population and clinical characteristics of subjects with LE are compared with those of subjects without LE. Unlike a report from the literature [2], there was no association between elevated body mass index (BMI) and the risk of LE in this study.

Table 5 **The LOGISTIC Procedure**

Analysis of Maximum Likelihood Estimates

Parameter	Wald Pr > ChiSq	Odds Ratio	95% Confidence Limits for Odds	
Intercept	0.0863	------	----------	----------
Control arm	0.2799	0.675	0.331	1.377
Ln submitted (>8)	<.0001	4.864	2.302	10.277
Ln positive (>0)	0.0171	2.505	1.177	5.329
Mastectomy (vs. other)	0.0754	0.507	0.240	1.072
Christian	0.0208	2.345	1.138	4.830

Table 6 Population Characteristics of Breast Cancer Survivors with and without Upper Extremity Secondary Lymphedema (LE) from the Walt Breast Center, Karmanos Cancer Institute, Detroit, MI

	With LE	Without LE	Univariate
N	87	71	
Mean age, yrs±SD(range)	53.5 ± 12.1 (29.3-80.2)	52.8 ± 11.2 (34.1-79.6)	P=0.7249
Gender (F, M)			
Race			
African American	36	32	P=0.6411
Caucasian	39	32	
Hispanic	3	0	
Arab/Chaldean	3	0	
Asian	1	3	
Native American	1	3	
Other	4	1	
Employment status			
Working	69	48	
Not working	16	20	
Retired	0	0	
Not answered	2	3	
Highest education level			P=0.7697 for college vs no college
Less than high school	10	7	
High school/GED	42	37	
Associate degree	0	0	
Bachelor degree	17	12	
Masters degree	5	6	
Doctorate/professional school	3	1	
Not answered	10	8	
Annual income			P=0.3775 for <$50,000 vs ≥ $50,001
< $5,000	6	8	
$5,000-$15,000	10	11	
$15,001-$30,000	10	8	
$30,001-$50,000	10	6	
$50,001-$75,000	10	7	
> $75,001	19	12	
Not answered	22	19	
Marital Status			
Married/Cohabitating	40	37	P=0.2646
Other responses	41	26	
Transportation			
Usually drive myself	58	46	P=0.8045
Other responses	29	25	
Religious Preference			
Christian	46	27	P=0.0378
Non-Christian	30	36	

Table 7 Clinical Characteristics of Breast Cancer Survivors with and without Secondary LE

	With LE	Without LE	Univariate
N	87	71	
Breast Cancer Stage			P=0.0241 For Stage 0,I vs IIA, IIB, IIIA, IIIB, IV
0	5	14	
I	26	24	
IIA	20	16	
IIB	20	9	
IIIA	9	6	
IIIB	7	2	
IV	0	0	
Type of breast surgery)			P=0.1705
Mastectomy with axillary surgery	47	41	
Lumpectomy with axillary surgery	36	22	
Lumpectomy	4	8	
Radiation therapy			P=0.5203
Yes	51	33	
No	36	38	
Number of LNs resected (mean ± SD)	11.1 ± 6.1	7.0 ± 5.7	P<0.0001
≤ 8 LNs submitted	29	48	P<0.0001
> 8 LNs submitted	58	23	
Number of LNs positive for ca (mean ± SD)	1.6 ± 3.0	1.0 ± 2.4	P=0.2795
0	45	52	P=0.0137
1-3	30	11	
>4	12	8	
Body Mass Index (BMI) (mean ± SD)	29.7 ± 7.1	28.8 ± 7.8	P=0.4443
BMI >25	49	64	P=0.5285
BMI >30	36	26	P=0.5422

Discussion: Univariate analysis of those with LE compared with those without LE in Tables 6 and 7 showed that LE was significantly associated with certain clinical characteristics. These included the number of mean number of lymph nodes resected at surgery (11.1 with LE vs 7.0 without LE, $p<0.0001$), especially if >8 lymph nodes were resected ($p<0.0001$). Furthermore, while the mean number of lymph nodes positive for metastatic cancer was not associated with increased risk for LE, the greater the number of lymph nodes positive for cancer (>4 vs 1-3 vs 0), the greater the risk of LE ($p=0.0137$). This is supported by the increased risk with higher stage of breast cancer (Stage IIA and above vs Stage 0 or I, $p=0.241$). The only population characteristic associated with those with LE was the religious preference of being a Christian. The reason for this is not determined.

For these interim data, there are new findings regarding the timing of LE occurrence which will be included in the final analysis of data next year.

From Fig. 1, the frequency of occurrence of LE was highest in the first year after surgery. LE occurring in the first year is acute LE. If it doesn't resolve, it becomes chronic. However, there were also subjects that had the LE occur after the first year. Therefore, a pattern of LE occurrence is an important finding of the study and has not been previously reported in the literature. There are several reasons for this, including lack of prospective data collection, and the frequency of measurements (quarterly) within this study that would not ordinarily occur in clinical practice. Table 8 describes the patterns of LE occurrence which is new information that will be put into a paper this coming year. There were 73 subjects with LE occurring within the first year after surgery. For 6 of these, the LE resolved within the first year. For another 6 subjects, the LE eventually resolved within 36 months. However, for the majority (61 subjects), the LE occurred during the first year after surgery and persisted. (All cases of LE were referred to the LE clinic for treatment.) These 61 cases of LE are now persistant and chronic.

There were 14 subjects in whom LE occurred after the first year after surgery. Only 1 resolved within 2 years, and 13 remain with chronic LE.

These patterns of LE occurrence are important for several reasons:

a) They show that careful postoperative measurements identify people with LE within the first year after surgery.
b) LE that occurs after the first year may be different from LE that occurs within the first year and gives support to further study of these differences.
c) The literature quotes 16-25.5% occurrence of LE in breast cancer survivors, with the greatest risk within 4 years of treatment[3,4] However, there is no distinction between acute and chronic LE. Therefore the quoted LE rate is not accurate since it mixes LE occurrence from different times postoperatively. Our rate for acute LE is 46.2%. Presentation of LE after the first year after surgery occurs in 8.9% of the study patients. There are 38.6% acute LE cases persisting to become chronic for a total chronic rate of 47.5%.

The plan is to continue to perform measurements and then specifically perform subset analysis looking at the influence of race, age, stage, type of surgery, number of lymph nodes removed and how many positive for cancer, and radiation therapy while examining LE cases as acute, chronic or acute becoming chronic (persistant).

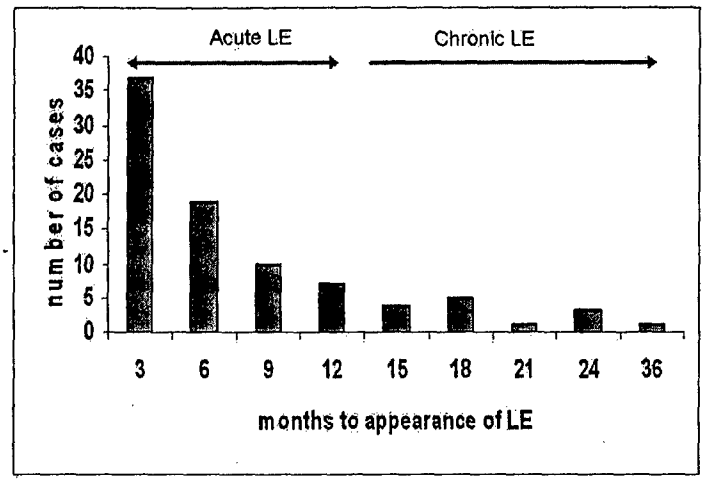

Fig. 1. Determining when secondary LE occurs after breast cancer surgery. Using quarterly prospective measurements after breast cancer surgery, secondary LE was determined by comparing volume changes to preoperative measurements. These were verified by a LE nurse specialist. The months to appearance of secondary LE are along the x-axis, and number of cases along the y-axis. By definition, acute LE presents and resolves within 12 months. Chronic LE presents after 12 months.

Table 8 Patterns of secondary LE presentation, resolution and persistence in upper extremity of breast cancer survivors

Presents within the first 12 months after surgery (73 cases)			
Secondary LE Pattern	**Time of occurrence/pattern description**	**N**	**Mean followup ± SD (mos)**
Acute LE only	**0-12 months** (Presents and resolves within 12 months after surgery)	**6**	**17.0 ± 10.3**
Acute LE→ chronic LE→ resolved	**0-12 month→resolved** (Presents within 12 months after surgery and resolves within 3 yrs)	**6**	**25.0 ± 10.3**
Acute LE→ chronic LE (persists)	**0-12 months→continues** (Presents within 12 months after surgery and persists) resolved)	**61**	**20.1 ± 12.0**
Presents more than 12 months after surgery (14 cases)			
Secondary LE Pattern	**Time of occurrence/pattern description**	**N**	**Mean followup (mos)**
Chronic LE only	**After 12 months** (Presents more than 12 months after surgery and persists)	**13**	**27.2 ± 8.1**
Chronic LE resolved	**After 12 months→resolved** (Presents more than 12 months after surgery and resolves within 3 yrs)	**1**	**30.0**
	Total	**87**	**19.3 ± 11.1**

Specific Aim 2) *What are the differences in the measured QOL among breast cancer patients during the first three years after surgery that received perioperative education in lymphedema protection as compared to a control group?*

For Specific Aim 2, there are 153 evaluable patients since 5 did not complete the QOL questionnaires preoperatively, and will not be part of Spec. Aim 2 analysis. Interim determination of changes in QOL can be determined with this number while the followup continues.

In Tables 9 and 10, the population and clinical characteristics of these 153 evaluable subjects are compared for the intervention and control groups.

Then in Table 11, the interim scores for the QOL instruments in this study are compared (FACT-B, MOS-SF36, and the sexuality and marital subscales of CARES). In Table 12, the interim longitudinal changes in the QOL scores are shown. In Table 13, the interim scores for the FACT-B subscales are shown that may give insight into the longitudinal changes in the FACT-B. In Table 14, the interim longitudinal change in the FACT-B scores are compared for the subscales.

Table 9 Population Characteristics of Study Participants in the Intervention and Control Groups for LE Protection teaching (Specific Aim 2)

	Intervention Group	Control Group
N	69	84
Mean age, yrs ± S.D.	53.4 ± 11.9	52.1 ± 11.2
Race		
African American	30	34
Caucasian	32	38
Hispanic	1	2
Arab/Chaldean	1	2
Asian	0	4
Native American	3	1
Other	2	3
Highest education level		
Less than high school	9	8
High school/GED	36	42
Associate degree	0	0
Bachelor degree	13	16
Masters degree	3	8
Doctorate/professional school	2	1
Not answered	6	9
Annual income		
< $5,000	5	8
$5,000-$15,000	9	12
$15,001-$30,000	7	10
$30,001-$50,000	8	8
$50,001-$75,000	8	9
> $75,001	15	15
Not answered	17	22
Marital Status		
Divorced/separated	17	17
Married/Cohabitating	33	33
Never married	8	11
Widowed	7	15
Not answered	4	8
Transportation		
Usually drive myself	43	58
Usually use public transportation	8	1
Usually driven by someone else	13	15
Other	0	2
Not answered	5	8
Religious Preference		
Catholic	18	17
Hindu	0	1
Jewish	2	0
Muslim	1	1
Protestant	18	18
Other	20	34
None	2	4
Not answered	8	9

Table 10 **Clinical Characteristics of Study Participants in the Intervention and Control Groups for LE Protection teaching (Specific Aim 2).**

	Intervention Group	Control Group
N	69	84
Breast Cancer Stage		
0	10	8
I	20	29
IIA	17	18
IIB	12	15
IIIA	6	9
IIIB	4	5
IV	0	0
Type of breast surgery)		
Mastectomy with axillary surgery	37	48
Lumpectomy with axillary surgery	27	30
Lumpectomy	5	6
Mean number of LN submitted	8.5 ± 5.8	9.9 ± 6.5
BMI (mean ± SD)	29.4 ± 7.4	29.3 ± 7.8

Table 11. **Interim QOL scores comparing the Intervention group with the Control group.**

	Intervention Group *n=71*		Control Group *n=87*	
	N		N	
FACT-B scores				
Total				
initial (mean)	65	122.06±6.49	79	105.19±3.90
6-month (mean)	46	129.54±10.86	49	113.19±4.88
12-month (mean)	32	132.08±11.85	48	115.42±3.68
24-month (mean)	17	129.68±17.70	19	135.86±13.69
36-month (mean)	6	99.67±18.26	13	128.15±9.66
MOS-SF 36 scores				
Physical Scale				
initial (mean)	60	46.06±1.44	70	47.92±2.20
6-month (mean)	45	43.05±6.06	48	28.24±8.48
12-month (mean)	33	48.25±3.50	44	44.41±1.53
24-month (mean)	18	46.38±2.24	18	47.62±2.05
36-month (mean)	7	45.91±4.34	12	47.81±2.41
Mental Scale				
initial (mean)	60	50.01±1.44	70	46.05±1.50
6-month (mean)	45	58.48±9.77	48	84.12±27.19
12-month (mean)	33	49.18±2.43	44	52.68±1.57
24-month (mean)	18	51.27±2.14	18	50.78±2.60
36-month (mean)	7	49.80±3.80	12	48.48±4.10

Table 11 (continued)

CARES scores

Sexuality Subscale				
initial (mean)	**54**	**7.39±3.07**	**65**	**25.05±13.07**
6-month (mean)	**38**	**77.55±33.84**	**43**	**26.56±15.43**
12-month (mean)	**26**	**43.39±26.68**	**34**	**68.85±34.90**
24-month (mean)	**10**	**77.90±37.87**	**10**	**5.90±2.46**
36-month (mean)	**3**	**5.33±2.73**	**4**	**123.75±107.52**
Marital Subscale				
initial (mean)	**54**	**23.796± 20.629**	**65**	**50.12±29.59**
6-month (mean)	**38**	**159.18±74.945**	**43**	**57.23±36.11**
12-month (mean)	**26**	**91.00±59.205**	**34**	**102.56±61.37**
24-month (mean)	**10**	**339.60±169.46**	**10**	**7.60±4.07**
36-month (mean)	**3**	**3.67± 2.33**	**4**	**420.25± 261.75**

Table 12 Interim Longitudinal changes in Quality of Life Scores for the Intervention Group and Control Group

	N	Intervention Group	N	Control Group
FACT-B (total score)				
6-mon compare to 0 month change	44	13.01±11.59	46	10.99±5.62
12-mon compared to 0 month	31	17.42±11.98	46	2.28±6.20
24-month compare to 0 month	17	16.85±18.51	18	26.64±12.88
36-month compared to 0-month	6	-26.44±16.26	11	18.89±9.88
MOS SF-36 (physical score)				
6-mon compare to 0 month change	39	-1.69±1.64	38	-9.36±5.26
12-mon compared to 0 month	29	-1.68±2.03	36	-5.26±4.49
24-month compare to 0 month	16	-3.86±2.30	14	3.28±2.17
36-month compared to 0-month	6	-0.44±2.92	11	4.78±2.82
MOS SF-36 (mental score)				
6-mon compare to 0 month change	39	-0.41±1.87	38	12.94±11.95
12-mon compared to 0 month	29	1.60±2.23	36	5.96±2.79
24-month compare to 0 month	16	3.08±3.02	14	-0.92±2.41
36-month compared to 0-month	6	-4.96±4.61	11	-1.31±5.13
CARES (sexuality subscale)				
6-mon compare to 0 month change	35	32.11±24.16	39	16.18±16.56
12-mon compared to 0 month	25	39.48±27.97	32	67.09±37.10
24-month compare to 0 month	10	75.80±37.38	10	0.10±3.53
36-month compared to 0-month	3	5.00±2.517	4	117.50±105.93
CARES (marital subscale)				
6-mon compare to 0 month change	35	83.63±59.24	39	26.95±28.73
12-mon compared to 0 month	25	90.36±61.74	32	103.44±65.37
24-month compare to 0 month	10	338.20±169.74	10	-5.50±4.86
36-month compared to 0-month	3	3.67±2.33	4	403.50±260.99

Notes: Please be aware that the following p-values are not statistically significant because of the number of tests that were run (p-values should be less than 0.0005 to be statistically significant.)

Total Fact B at baseline	Intervention (122)	Control (105)	p-value=0.0280
MOS-SF 36 Mental at baseline	Intervention (50)	Control (46)	p-value=0.0615
CARES Sexuality at 24 months	Intervention (78)	Control (6)	p-value=0.0900
CARES Marital at 24 months	Intervention (340)	Control (8)	p-value=0.0818
For those who answered 75% or more of the questions			
CARES Sexuality at 24 months	Intervention (110)	Control (7)	p-value=0.0837
Dif. in Fact B 0 – 36 months	Intervention (-26)	Control (19)	p-value=0.0230
Dif. in MOS-SF 36 Physical 0 – 24 months	Intervention (-4)	Control (3)	p-value=0.0335
Dif. in CARES Sexuality 0 – 24 months	Intervention (76)	Control (0)	p-value=0.0741
Dif. in CARES Marital 0 – 24 months	Intervention (338)	Control (-6)	p-value=0.0736
MOS-SF 36 Mental at baseline	Lumpectomy (50)	Mastectomy (46)	p-value=0.0582
Dif. in Mental 0 – 12 months	Lumpectomy (-1)	Mastectomy (9)	p-value=0.0088
CARES Dif. in Sexuality 0 – 24 months	Lumpectomy (54)	Mastectomy (0)	p-value=0.0775

Discussion: From Table 11 and Table 12, The scores for the intervention group and the control group do not differ for this first level of analysis. This is expected if the prospectively randomized patients are to be compared. However, the impact of LE teaching on QOL is not determined without including the time of the LE diagnosis. This may impact on the QOL scores as was presented in the preliminary data for the grant. Therefore, the plan for the final analysis is to determine the changes in QOL scores based upon the time of LE diagnosis. This was tested in the data analysis for knowledge and compliance with protection methods to be presented next for Specific Aim 3. Therefore, it will be feasible for the QOL data analysis.

The CARES questionnaire has been particularly problematic with some of the subjects due to questions regarding marital and sexual relationships. Although these are not as detailed as other questionnaires, we observe that patients do not answer questions on the CARES questionnaires because they may not be in a relationship at the time. That is why the analysis examines those who have answered at least 75% of the questions in order to have meaningful data about those questions. At the same time, the number of subjects who feel they cannot respond to the questions is also noteworthy.

The following subscale analysis for FACT-B presented in Tables 13 and 14 also do not identify significant differences between the intervention group and the control group. This would be expected in a prospective randomized trial. However, specific attention to the time of diagnosis of LE in these analysis is planned.

Table 13 Interim Subscale Scores for the FACT-B QOL Questionnaire comparing the Intervention Group with the Control Group

		Intervention Group *n=71*		Control Group *n=87*
	N		N	
FACT-B subscales				
Breast				
initial (mean)	65	28.17±1.73	79	22.10±2.63
6-month (mean)	46	27.37±3.61	49	24.82±0.93
12-month (mean)	32	25.91±0.93	48	24.98±1.21
24-month (mean)	17	24.96±1.74	19	29.83±5.33
36-month (mean)	6	26.00±1.86	13	26.16±1.65
GP (Physical)				
initial (mean)	65	20.69±2.16	79	9.59±8.87
6-month (mean)	46	23.08±0.70	49	21.63±0.79
12-month (mean)	32	23.22±0.92	48	21.96±1.47
24-month (mean)	17	22.72±1.21	19	24.63±0.74
36-month (mean)	6	7.83±17.03	13	24.62±1.08
GS (Social)				
initial (mean)	65	30.78±4.82	79	39.01±11.18
6-month (mean)	46	38.68±7.86	49	28.44±3.83
12-month (mean)	32	39.30±9.14	48	27.00±2.30
24-month (mean)	17	28.25±5.68	19	37.45±11.38
36-month (mean)	6	24.17±1.45	13	33.91±8.45
GE (Emotional)				
initial (mean)	65	18.65±0.53	79	15.83±1.46
6-month (mean)	46	17.18±2.18	49	18.82±0.69
12-month (mean)	32	19.16±0.82	48	20.17±0.67
24-month (mean)	17	-4.94±23.21	19	20.42±0.71
36-month (mean)	6	20.87±0.97	13	19.92±0.72
GF (Functional)				
initial (mean)	65	23.78±2.04	79	18.67±0.82
6-month (mean)	46	23.24±2.35	49	19.49±1.02
12-month (mean)	32	24.50±3.38	48	21.32±0.86
24-month (mean)	17	58.71±39.69	19	23.53±1.10
36-month (mean)	6	20.81±1.98	13	23.54±1.73

Table 14 Interim Longitudinal changes in FACT-B Subscale scores for the Intervention group compared with the Control group.

	N	Intervention group	N	Control group
FACT-B (Breast Subscale)				
6-mon compare to 0 month change	44	1.71±3.71	46	0.75±1.06
12-mon compared to 0 month	31	-1.09±1.09	46	3.21±4.28
24-month compare to 0 month	17	-0.15±2.37	18	4.08±5.65
36-month compared to 0-month	6	-4.63±0.98	11	0.64±2.21
FACT-B (GP Subscale)				
6-mon compare to 0 month change	44	1.42±2.29	46	3.35±2.36
12-mon compared to 0 month	31	-0.87±0.78	46	4.49±3.40
24-month compare to 0 month	17	-1.13±1.02	18	1.99±1.17
36-month compared to 0-month	6	-18.23±17.37	11	3.36±2.03
FACT-B (GS Subscale)				
6-mon compare to 0 month change	44	11.18±8.83	46	4.24±4.63
12-mon compared to 0 month	31	15.11±9.54	46	-10.62±13.00
24-month compare to 0 month	17	3.19±5.58	18	15.79±11.57
36-month compared to 0-month	6	-2.75±1.68	11	10.44±9.58
FACT-B (GE Subscale)				
6-mon compare to 0 month change	44	-1.39±2.31	46	1.58±0.76
12-mon compared to 0 month	31	0.87±0.82	46	3.89±2.52
24-month compare to 0 month	17	-23.12±23.02	18	2.78±1.09
36-month compared to 0-month	6	0.87±0.47	11	1.91±1.16
FACT-B (GF Subscale)				
6-mon compare to 0 month change	44	0.09±3.15	46	1.08±1.09
12-mon compared to 0 month	31	3.40±3.47	46	1.32±1.07
24-month compare to 0 month	17	38.06±40.09	18	2.00±0.80
36-month compared to 0-month	6	-1.69±1.815	11	2.55±1.04

Notes: Please be aware that the following p-values are not statistically significant because of the number of tests that were run (p-values should be less than 0.0005 to be statistically significant.)

Breast Subscale at baseline	Intervention (28)	Control (22)	p-value=0.0563
GE Subscale at baseline	Intervention (19)	Control (16)	p-value=0.0724
GF Subscale at baseline	Intervention (24)	Control (19)	p-value=0.0224
Dif. in Breast 0 – 36 months	Intervention (-5)	Control (1)	p-value=0.0483
Dif. in GF 0 – 36 months	Intervention (-2)	Control (3)	p-value=0.0444
Dif. in GP 0 – 24 months	Intervention (-1)	Control (2)	p-value=0.0540

Breast Subscale at 36 months	Lumpectomy (28)	Mastectomy (23)	p-value=0.0438
GF Subscale at baseline	Lumpectomy (23)	Mastectomy (19)	p-value=0.0541
Dif. in GF Subscale 0 – 6 months	Lumpectomy (-3)	Mastectomy (3)	p-value=0.0874

Specific Aim 3) *What are the retention of information on lymphedema protection, and the compliance with arm precautions among breast cancer patients who received perioperative lymphedema training as compared to a control group?*

The knowledge questionnaires are given preoperatively and at 6 months, 12 months, 24 months and 36 months after surgery. There are 17 questions that cover several categories of protection methods to reduce the risk of LE. The compliance questionnaires are given at the same intervals as the knowledge questionnaires with the exception that no preoperative compliance questionnaire is given. There are 22 questions with each scored from 0 to 4 depending on the frequency of use of a particular protection method.

In Table 15, the interim scores for the knowledge and compliance questionnaires are compared for the intervention and control groups. These are not significantly different. However, in Table 16, the scores are compared for those with LE as compared to those without LE. In addition, the time of LE diagnosis was included so that those with LE at the time of the questionnaire were listed as LE positive. Then for each interval the number of subject who with or without LE changes as new cases are diagnosed (and some resolve). Still required is determining the scores for those with and without LE within the intervention and control groups. This will be a more precise method of reporting the impact of teaching on LE occurrence. We plan to continue these analyses as data are collected.

Table 15. Interim analysis of knowledge and compliance questionnaires for the Intervention Group and Control Group (Specific Aim 3)

		Intervention Group *n=71*		**Control Group** *n=87*
	N		**N**	
Knowledge Questionnaire				
Pretest (mean)	**58**	**0.35±0.04**	**71**	**0.37±0.04**
6-month (mean)	**46**	**0.67±0.04**	**51**	**0.67±0.04**
12-month (mean)	**30**	**0.78±0.05**	**44**	**0.74±0.04**
24-month (mean)	**19**	**0.82±0.06**	**19**	**0.73±0.06**
36-month (mean)	**5**	**0.76±0.15**	**12**	**0.79±0.06**
Dif. Pre Post	**39**	**0.37±0.06**	**41**	**0.26±0.05**
Compliance Questionnaire		**Intervention**		**Control**
6-month (mean)	**42**	**3.22±0.09**	**46**	**3.12±0.12**
12-month (mean)	**31**	**2.98±0.16**	**46**	**3.04±0.10**
24-month (mean)	**16**	**2.92±0.15**	**19**	**3.10±0.14**
36-month (mean)	**7**	**2.87±0.32**	**11**	**2.96±0.18**

Table 16 **Interim analysis of knowledge and compliance questionnaires for those with LE and those without LE (Specific Aim 3)**

		Without LE		With LE
	N		N	
Knowledge Questionnaire				
6-month (mean)	59	0.65±0.04	38	0.70±0.04
12-month (mean)	41	0.71±0.04	33	0.81±0.04
24-month (mean)	17	0.72±0.08	21	0.82±0.04
36-month (mean)	4	0.57±0.15	13	0.85±0.05
Dif. Pre Post	47	0.32±0.05	33	0.30±0.06
Compliance Questionnaire				
6-month (mean)	51	3.09±0.11	37	3.27±0.11
12-month (mean)	41	2.90±0.11	36	3.14±0.14
24-month (mean)	15	2.76±0.15	20	3.22±0.12
36-month (mean)	6	2.43±0.27	12	3.17±0.17

Notes: Please be aware that the following p-values are not statistically significant because of the number of tests that were run (p-values should be less than 0.0005 to be statistically significant.)

Knowledge at 36 months	Lymphedema- (0.57) Lymphedema+(0.85)	p-value=0.0413
Compliance at 24 months	Lymphedema- (2.76) Lymphedema+(3.22)	p-value=0.0204
Compliance at 36 months	Lymphedema- (2.43) Lymphedema+(3.17)	p-value=0.0269

Task 12. **Analysis of data after 5th year, Months 61-65.**

Not yet applicable.

Task 13. **Annual report to USAMRMC, Months to be designated by USAMRMC.**

Year I, Year II and Year III and Year IV reports submitted.

Task 14. **Meeting in Baltimore, Maryland to disseminate results of DoD-sponsored Research during the second year, Month to be announced by USAMRMC.**

Attended September, 2003, Orlando, FL. Poster presentation.

Task 15. **Write journal articles. Submit abstract, Months 12-60+**

This is ongoing. We are preparing a paper describing the patterns of LE. Further QOL analysis will be performed during the year so that the data can be more quickly evaluated at the end of the next year for the final report.

During this fourth annual year report, the Tasks in the Statement of Work are being accomplished and data are being collected as described in the study. The data are being collected around each of the specific aims of the study. The Specific aims will be answered when all followup data still being collected in the firth year will be analyzed for a final report.

KEY RESEARCH ACCOMPLISHMENTS

- **Patterns of lymphedema are identified: acute LE cases that persist past the first year after surgery, and chronic LE cases that present after the first year from surgery. Paper in preparation.**
- **Knowledge of and compliance with LE protection methods depend on the time of occurrence of LE**

REPORTABLE OUTCOMES

Presentation (Poster)
"Equality in Male Breast Cancer Care using Sentinel Lymph Node Biopsy", presented at the 2004 national meeting of the Association of VA Surgeons, Richmond Virginia (May, 2004).

Funding Applied
NIH: Linking Lymphedema to Disorders of Lymphangiogenesis (PI: Kosir) (Pending)
Komen: Linking Lymphedema to Disorders of Lymphangiogenesis (PI: Kosir)(Pending)
VACO: Linking Lymphedema to Inherited Disorders of Lymphangiogenesis (PI: Kosir) (Pending)

CONCLUSIONS

The identification of LE has been shown to require attention to measurement changes even during the first year after surgery. This pattern of LE occurrence leads to a persistant problem in a majority of patients. In this interim report, we have identified an overall LE rate of 55%. To be more precise, our rate for acute LE is 46.2%. Presentation of LE after the first year after surgery occurs in 8.9% of the study patients. There are 38.6% acute LE cases persisting to become chronic for a total chronic rate of 47.5%. This means that the problem of LE is a significant problem. The identification of newer treatment plans and modalities that may obviate the need for injury to the lymphatics would help reduce the incidence of LE.

"So What Section"

The awareness of lymphedema occurrence, protection, and treatment by many clinicians that are in contact with breast cancer survivors is not uniform. Furthermore, textbooks do not include enough detail regarding incidence, symptoms, measurement, and treatment, which lead to less attention to the

survivor's observations. This study must be completed to rebut current opinion in the medical literature. It will "rock the boat" and challenge current practice. Already, lymphedema in the first year postoperatively is underreported and this study will be able to add to the literature. We have already published a comparison of methods in detecting LE using our own rigorous detection as the "standard". The longitudinal collection of measurements in several dimensions (physical, quality of life, knowledge, behavior (compliance)) will provide strong data and conclusions that are absolutely necessary to shift established practices that have not really been the result of careful study. There are also several additional studies that will emanate from this study, with the potential to include additional disciplines in breast cancer research.

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APPENDIX

Appendix Item 1- Task 4 Perioperative teaching session

Appendix Item 2- Task 5 Arm measurements

Appendix Item 3- Task 7 Booster teaching session

Appendix Item 4- Task 9 Weekly volume report

Appendix I

Task 4 **Perioperative teaching sessions (Intervention group)** **n=71**

ID	Type of Surg	Initial Class
6	M+L	x
7	L+L	x
9	L+L	x
13	L+L	x
15	M+L	x
19	L+L	x
21	M+L	x
26	M+L	x
28	M+L	x
29	L+R	x
33	L+L	x
35	L+R	x
40	M+L	x
42	L+L	x
46	M+L	x
47	M+L	x
51	L+L	x
55	M+L	x
56	L+R	x
57	M+L	x
58	L+L	x
59	L+L	x
60	L+L	x
62	M+L	x
67	L+L	x
73	L+L	X
74	L+L	x
77	L+L	X
78	M+L	X
84	M+L	X
85	M+L	X
86	M+L	X
90	L+L	X
92	M+L	X
93	M+L	X
97	L+L	X
98	L+L	X
111	M+L	X
113	L+L	X
114	M+L	X
117	M+L	X
118	L+R	X
120	L+L	X
122	L+L	x
124	L+L	x
128	M+L	x
132	M+L	x
133	M+L	x
134	M+L	x
136	M+L	x
139	M+L	x
146	M+L	x
150	L+R	x
153	M+L	x
157	M+L	x
158	M+L	x
160	M+L	X
161	L+L	X
164	M+L	X
165	M+L	X
168	L+L	X
175	M+L	x
176	L+L	x
177	L+L	x
179	M+L	x
184	M+L	X
186	M+L	X
188	M+L	X
189	L+L	X
190	L+L	X
194	M+L	X

just three pages of the 30 page document are shown here for example.

Patient Number	Interval	Current Weight	Affected Arm	Height	Handedness	Affected 1st Finger	Affected Hand (A)	Affected Wrist (B)	Affected 10 cm (C)	Affected 20 cm (D)	Affected Elbow (E)	Affected 30 cm (F)	Affected 40 cm (G)	Affected Grip	Affe Exte
001	0	305	L	64	R	7.00	19.00	18.40	24.50	30.50	31.50	36.80	52.80	normal	180
001	3	302	L	64	R	7.50	20.00	18.30	23.50	31.00	33.00	39.30	51.00	normal	180
001	6	309	L	64	R	7.50	20.00	18.00	23.00	29.00	31.00	34.00	48.00	normal	180
001	15	309	L	64	R	7.50	20.50	17.80	23.60	29.50	30.50	35.80	49.80	normal	180
001	24	265	L	64	R	7.40	20.00	17.40	22.50	27.90	29.00	33.50	46.80	50	180
001	36	180	L	64	R	7.00	19.30	16.20	19.80	24.70	25.40	29.10	37.80	normal	180
002	0	172	R	61	R	6.40	19.40	15.50	23.90	28.60	27.50	32.60	37.80	normal	180
002	3	160	R	61	R	6.50	19.70	16.00	23.30	28.70	28.50	31.00	37.70	normal	180
002	6	158	R	61	R	7.10	19.80	16.70	22.00	28.00	27.90	30.50	36.50	normal	180
002	9	155	R	61	R	6.80	19.00	16.40	27.90	27.90	27.40	30.00	35.90	normal	180
002	12	172	R	61	R	6.80	19.00	16.10	22.70	27.80	27.00	29.70	36.00	normal	180
002	24	167	R	61	R	7.00	19.50	16.30	27.90	28.70	29.90	34.30	39.20	15	180
002	33	172	R	61	R	6.80	19.20	16.30	25.30	28.40	27.90	32.40	36.60		180
002	36	164	R	61	R	6.90	18.90	15.90	23.80	28.00	28.00	30.40	37.90	60	180
004	0	127	R	54	R	5.50	19.00	14.30	17.40	22.80	22.80	22.50	25.80	normal	180
004	3	118	R	53.5	R	5.40	17.50	14.80	15.70	20.80	22.00	21.50	24.00	normal	180
004	12	127	R	53.5	R	6.10	18.50	14.50	16.50	21.60	23.00	22.00	23.50	38	180
005	0	226	L	63.75	R	7.10	20.70	17.50	22.10	28.40	27.80	31.80	40.80	normal	180
005	3	229	L	63.75	R	5.50	18.60	15.60	20.60	26.50	26.30	29.70	37.90	normal	180
005	6	224	L	63.25	R	6.40	17.00	16.00	20.00	27.00	26.70	29.00	36.00	abnormal	180
005	9	224	L	63.75	R	6.40	17.00	16.00	20.00	27.00	26.70	29.00	36.00	abnormal	180
005	12	227	L	63.75	R	6.40	20.60	16.00	20.00	27.00	27.00	29.60	37.00	45	180
005	15	226	L	63.75	R	6.40	20.00	16.10	21.10	27.30	26.80	30.70	39.00	normal	180
006	0	185	R	64	R	7.50	20.30	16.50	22.00	27.90	27.90	29.10	33.50		180
006	6	190	R	64	R	6.50	20.00	17.00	21.00	29.00	28.00	28.90	34.70	normal	180
006	12	183	R	64	R	6.50	20.40	16.00	20.60	27.50	27.00	28.30	32.50	normal	180
007	0	180	R	64	R	7.50	20.00	18.00	22.60	22.60	28.20	30.00	33.00		180
007	3	170	R	63.5	R	7.00	18.80	16.00	18.00	24.30	26.00	26.50	31.00	normal	180
007	6	170	R	64	R	6.80	18.40	15.90	17.90	24.00	24.40	24.70	27.00	normal	180
007	12	170	R	64	R	6.90	18.10	15.10	17.90	23.50	24.50	24.70	28.40	normal	180
007	24	167	R	64	R	7.00	18.60	15.50	18.90	24.20	25.00	25.10	30.00	40	180
007	36	176	R	64	R	7.00	18.00	15.40	20.40	25.00	25.00	26.80	31.90	50	180
007	67	177	R	63.5	R	6.90	18.50	15.50	20.70	25.70	25.50	27.90	32.20	normal	180
008	0	107	L	62	R	5.90	15.40	13.80	16.00	21.50	21.00	23.00	26.00	normal	90

008	3	107	L	62	R	5.70	17.50	13.90	15.70	21.70	20.80	22.80	24.50	abnormal	
008	6	107	L	62	R	6.00	17.00	13.80	16.00	22.00	21.60	21.00	25.50	abnormal	180
008	12	107	L	62	R	5.70	16.60	13.80	15.60	21.70	20.80	21.70	25.40	normal	45
008	15	110	L	62	R	5.80	17.00	13.60	15.80	21.40	20.60	22.50	26.50	normal	180
008	18	111	L	62	R	5.60	17.00	13.50	16.00	21.40	20.80	23.10	26.60	normal	180
009	0	183	R	66	R	6.50	20.80	16.00	23.00	28.00	27.00	33.00	36.00	normal	180
009	3	192	R	66	R	6.50	20.50	17.00	21.00	27.50	28.60	31.00	36.50	normal	180
009	6	195	R	65	R	6.50	19.80	16.50	21.40	28.00	29.00	31.50	38.70	normal	180
009	12	196	R	65	R	6.40	20.20	16.20	22.00	28.00	28.50	32.00	39.00		180
009	15	196	R	65	R	6.50	20.10	16.10	22.80	29.70	28.60	33.40	39.50	normal	180
009	21	195	R	65	R	6.40	20.40	16.60	21.30	27.30	27.40	30.60	37.10	normal	norm
011	0	216	R	63.75	R	8.00	21.00	18.70	28.00	34.00	32.50	37.70	40.50	normal	180
011	3	198	R	64	R	8.00	21.00	18.90	25.90	32.00	31.00	35.00	42.80	abnormal	90
011	6	198	R	64	R	4.30	16.80	15.20	25.30	28.60	27.60	34.20	40.50	abnormal	90
011	9	198	R	64	R	7.50	20.50	18.50	25.40	31.70	31.50	33.90	41.10	25	90
011	12	191	R	63.75	R	7.80	20.70	17.90	25.10	31.20	30.00	34.40	39.50	normal	90
011	18	184	R	65	R	7.80	20.80	17.80	24.90	31.10	29.80	34.60	39.60	normal	90
011	24	214	R	64	R	7.50	21.10	17.90	26.00	31.30	28.90	35.20	41.30		180
012	0	138	R	63	R	6.70	19.70	15.00	19.50	25.00	26.50	26.70	30.00	normal	180
012	3	141	R	63	R	6.70	18.00	16.00	18.80	25.40	26.70	26.70	30.00	normal	180
012	6	142	R	63	R	6.50	18.90	16.00	19.90	25.90	27.00	27.00	29.90	normal	180
012	9	140	R	63	R	6.70	18.80	15.50	20.00	26.00	26.40	27.10	31.40	42	180
012	12	141	R	63	R	6.60	19.60	15.20	20.00	25.50	26.60	27.00	30.00	45	180
012	15	142	R	63	R	6.50	19.30	15.40	21.70	25.60	26.50	27.20	29.80	normal	180
012	24	140	R	63	R	6.90	18.50	15.60	20.20	25.40	26.50	26.80	30.00	60	180
012	36	140	R	63	R	6.60	18.70	15.90	20.70	25.60	27.00	27.40	30.40	55	180
012	67	140	R	63	R	6.60	18.70	15.40	20.70	25.60	26.30	27.40	30.20		
013	0	205	R	69	R	6.50	19.90	16.50	18.50	24.90	28.90	27.00	31.00	normal	180
013	3	205	R	69	R	6.70	19.50	16.30	19.20	26.20	27.20	34.60	37.70	normal	180
014	0	120	L	64	R	5.80	17.30	14.90	17.90	22.30	21.90	21.10	23.90	normal	180
014	3	120	L	64	R	6.40	18.00	15.40	17.90	22.70	22.00	22.20	24.00	normal	180
014	6	125	L	64	R	6.50	17.50	15.50	17.90	23.00	23.00	22.70	24.50	normal	180
014	12	125	L	65	R	6.60	18.00	15.30	18.60	23.40	22.60	23.40	24.90	normal	90
014	15	129	L	64.5	R	6.30	17.80	15.60	18.40	23.50	23.20	23.50	25.50	normal	180
014	24	120	L	64	R	6.30	18.60	15.30	18.80	23.20	23.00	23.10	25.90		180
014	30	134	L	64	R	6.40	17.90	15.40	18.50	23.40	23.00	23.30	25.00	45	180
014	36	124	L	64	R	6.40	17.90	15.40	18.50	23.00	22.90	23.70	25.00	50	
015	0	135	L	69	R	6.40	18.80	16.00	16.00	22.70	23.50	22.20	25.00	normal	180
015	3	132	L	69	R	5.80	18.50	15.50	15.80	22.00	22.00	22.00	23.80	normal	180
015	6	135	L	69	R	5.80	18.40	15.60	16.00	22.50	23.00	22.00	24.40	normal	180

015	9	137	L	69	R	5.80	18.40	15.60	16.50	23.10	23.70	22.50	25.00	normal	
018	0	143	R	66.5	R	6.70	19.00	15.00	17.00	23.50	23.70	22.80	28.50	normal	180
018	3	148	L	66.5	R	6.10	18.70	15.00	17.70	24.00	23.00	23.00	27.40	abnormal	90
018	12	147	R	66.5	R	5.90	19.00	14.90	17.60	24.10	23.90	23.40	27.80	55	180
019	0	145	L	65	R	6.00	18.00	15.00	18.50	25.00	25.00	24.50	27.40		180
019	3	145	L	65	R	6.00	18.50	14.90	17.40	23.40	24.00	23.40	26.00	normal	180
019	6	149	L	65	R	5.80	18.30	15.00	18.80	25.00	24.90	26.00	29.00	normal	180
019	9	145	L	65	R	5.90	18.50	15.00	18.40	24.70	25.00	25.70	29.00	normal	90
019	12	150	L	65	R	5.80	18.90	14.80	17.80	24.30	24.40	24.50	28.30	78	180
019	24	136	L	65	R	5.70	18.00	14.70	18.50	23.90	23.50	23.40	26.50	65	180
019	36	142	L	65	R	6.00	18.50	14.80	18.40	24.10	23.70	24.00	27.30	65	180

Appendix 3

Task 7 **Booster Training Session for Group 1 subjects (n=71)**

ID	Booster
6	x
7	x
9	x
13	
15	x
19	x
21	x
26	x
28	X
29	x
33	x
35	x
40	X
42	x
46	x
47	X
51	X
55	x
56	X
57	X
58	x
59	X
60	x
62	x
67	x
73	x
74	x
77	X
78	X
84	x
85	
86	x
90	
92	
93	x
97	x
98	x
111	X
113	X
114	
117	
118	
120	
122	x
124	x
128	x
132	x
133	X
134	x
136	x
139	
146	x
150	x
153	x
157	x
158	X
160	X
161	X
164	X
165	X
168	X
175	x
176	x
177	x
179	x
184	
186	
188	
189	
190	
194	

Task 9 **Calculation of Limb Volumes and comparison of** **rı differences**

volume % changes compared to preop measurements

[redacted] yellow color = >9% vol change, LE- [redacted]

green text = >10% vol chg, confirmed LE- by CR eval

[redacted]														
004	1	-11.43%			-7.19%									
005	2	-13.64%	-16.42%	-16.42%	-13.29%	-8.35%								
006	2		1.61%		-6.04%									
007	1	-15.95%	-14.13%		-14.22%				-8.27%				-0.32%	
[redacted]														
015	1	-6.05%	-2.82%	1.62%										
018	2	0.07%			2.30%									
[redacted]														
020	2		4.22%	4.89%	1.11%									
021	1	8.56%	4.42%											
[redacted]														
025	1	7.71%	7.71%		1.81%									
[redacted]														
034	2	4.12%			3.07%									
035	1		9.14%											[redacted]
[redacted]														
050	2	4.76%			1.99%		6.35%						4.20%	
051	1		3.50%		8.51%		8.51%		8.22%				4.80%	
053	2		-12.27%											

Appendix 4

Task 9 **Calculation of Limb Volumes and comparison of n differences**

volume % changes compared to preop measurements

yellow color = >9% vol change, LE-

orange color = new to this report

green text = >10% vol chg, confirmed LE- by CR eval

056	1	1.13%			0.21%					8.92%				
057	1	-2.36%				-1.91%			-3.44%					
061	2		-6.22%											
065	2		1.06%											
071	2		4.64%		-13.89%									
072	1				6.19%			3.20%	-4.16%		4.19%			
073	1		-4.47%	-3.38%										
075	2								-13.84%					
076	2	6.42%	-1.25%							-2.25%				
081	2			-3.84%										
084	1		-1.72%		-2.44%				3.24%		-0.03%	1.77%		
085	1										-35.27%			
088	2				3.13%									
092	1			3.75%			-8.20%							
092	1			3.75%			-4.76%							
093	1		-1.37%				-3.63%		1.11%		0.73%			
094	2				5.23%									
099	2			-4.20%				-3.64%			-2.43%			
100	2		6.51%						0.23%			-10.93%		

Task 9 **Calculation of Limb Volumes and comparison of π differences**

volume % changes compared to preop measurements

yellow color = >9% vol change, LE-

green text = >10% vol chg, confirmed LE- by CR eval

104	1	7.52%					0.91%							
105	2						4.02%				15.08%			
107	2	8.61%			-0.46%	2.94%	-3.14%							
109	2			-12.92%										
111	1	6.82%			13.09%									
115	2	-0.93%			3.91%			5.64%						
116	2				5.72%		7.05%		9.82%					
117	1								18.60%					
118	1			4.39%	4.13%									
120	1			-0.93%	-4.52%	-3.77%	-3.45%		2.20%					
123	2				1.30%		2.13%		4.31%					
125	2			-14.23%										
129	2	-6.63%						-4.45%						
132	1						-2.44%	1.23%						
134	1		-6.07%		-1.69%									
138	2				5.05%									
139	1		-5.46%											
140	2		-2.02%	-2.80%		7.47%								
141	2		4.73%		4.58%	7.67%	21.97%							
142	2	-6.62%		-6.01%		-8.32%								
147	2	0.99%												
148	1	-9.70%		-12.28%	-5.35%	-1.40%								

Task 9 **Calculation of Limb Volumes** ***and comparison of n differences***

volume % changes compared to preop measurements

yellow color = >9% vol change, LE- orange color = new volume report

green text = >10% vol chg, confirmed LE- by CR eval

149	1			3.49%		2.39%	-5.55%							
150	1	-4.88%	-5.52%	2.25%			-1.58%							
153	1		3.52%			0.59%								
155	1		-3.21%	-5.83%		-9.13%								
156	2	5.49%												
158L	1	-14.35%			-5.20%									
158R	1	0.20%			-2.49%									
159	2		-2.30%		-2.12%									
160	1		-6.88%											
161	1	2.62%	0.20%											
167	2				14.32%									
169	2			-0.71%										
175	1	-2.61%	3.79%											
177	1	3.04%		-7.32%										
182	2		0.79%											
185	2	-0.35%	-1.92%											
189	1	-2.72%												
194	1	-3.28%												